

2018 IMAG Futures Meeting – Moving Forward with the MSM Consortium (March 21-22, 2018)

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Institution(s): UCSF, California Medical Innovations Institute and Stanford University

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Title of Grant: Multi-Scale Laws of Myocardial Growth and Remodeling

Abstract Authors

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Abstract Text

Heart failure (HF) is a worldwide epidemic that contributes considerably to the overall cost of health care in developed nations. The overall goals of our grant are to identify the mechanical culprits that dictate the bifurcation of the system from the stable healthy state into the unstable state of HF and to determine the borderline between physiological/compensatory and pathophysiological/non-compensatory growth and remodeling. To address these goals, our research approach is to experimentally inform and validate multi-scale laws of myocardial growth and remodeling using three different clinically relevant large animal HF preparations in order to predict the propensity of patients with a myocardial infarction developing HF.

Using high resolution *ex vivo* data, we constructed a precise fully subject-specific biventricular finite-element model of healthy and failing swine hearts. Each model includes fully subject-specific geometries, myofiber architecture and, in the case of the failing heart, fibrotic tissue distribution. Passive and active material properties are prescribed using hyperelastic strain energy functions that define a nearly incompressible, orthotropic material capable of contractile function. These materials were calibrated using a sophisticated multistep approach to match orthotropic tri-axial shear data as well as subject-specific hemodynamic ventricular targets to ensure realistic cardiac function. Each mechanically beating heart is coupled with a lumped-parameter representation of the circulatory system, allowing for a closed-loop definition of cardiovascular flow. The circulatory model incorporates unidirectional fluid exchanges driven by pressure gradients of the model, which in turn are driven by the mechanically beating heart. This creates a computationally meaningful representation of the dynamic beating of the heart coupled with the circulatory system. Each model was calibrated using subject-specific clinical data and compared with independent *in vivo* strain data obtained from echocardiography. Our methods produced highly detailed representations of swine hearts that function mechanically in a remarkably similar manner to the *in vivo* subject-specific strains on a global and regional comparison. The degree of subject-specificity included in the models represents a milestone for modeling efforts that captures realism of the whole heart. This study establishes a foundation for future computational studies that can apply these validated methods to advance cardiac mechanics research.

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